

respectfully traversed. The rejected claims are presented to cover the oral formulations of this invention. As described in the specification as originally filed (see the paragraphing bridging pages 4 and 5), these formulations can be orally administered in a total daily dosage of up to 600 mg. of a compound of formula I and up to 300 mg. of diuretic. This provides the basis for the upper limit of each range given in claim 13 as amended. The specification also teaches (see the paragraph bridging pages 4 and 5) that the formulation of this invention can be administered once daily or in divided doses. The use of a dosage of as little as 5 mg. of a compound of formula I and as little as 2.5 mg. of a diuretic is taught. This provides the basis for the lower limit of each range given in claim 13 as amended. Further support for the lower limits of each range can be found in original claims 23 and 24.

In making his rejection, the Examiner has taken the position "While the various end points claimed are found in the specification it is apparent from the original disclosure that they refer to two distinct formulations with differing amounts." All of Applicants' disclosed formulations contain a compound of formula I and a diuretic. The rejected claims (13 and 15 to 20) do not cover "distinct formulations"; to present multiple claims to cover a single type of formulation would serve no useful purpose.

All of the claims in this application (claim 1 and 3 to 25) stand rejected under 35 U.S.C. 103 "as being obvious over Ondetti et al in view of Johnson et al for reasons of record". Referring first to paper no. 3 (the Examiner's "first action") it is suggested that the Examiner has incorrectly described references R (Ondetti et al) and S (Johnson et al). It is Johnson et al that teaches a combination of SQ 20,881 and

lower is
single
dose
upper
daily

frusemide, not Ondetti et al. The Examiner has apparently taken the position that SQ 20,881 and the proline derivatives of Applicants' formula I are equivalent. Therefore, according to the position of the Examiner, it would be obvious to substitute a proline derivative of Applicant's formula I for SQ 20,881 in the composition of Johnson et al comprising SQ 20,881 and a diuretic.

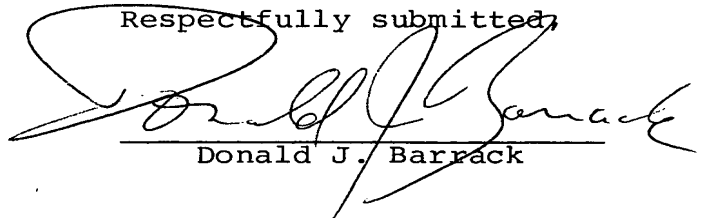
It is respectfully submitted that SQ 20,881 and the proline derivatives of Applicants' formula are not equivalent. In dismissing Applicants' previous arguments relating to lack of equivalence the Examiner states "Applicants' comments concerning the mode of administration are not well taken since it has not been shown that SQ 20,881 is inactive when taken orally." The Examiner's attention is directed to column I of the Ondetti et al reference where it is stated "Preliminary studies [reference omitted] have demonstrated the great potential of SQ 20,881 as a novel antihypertensive drug, limited only by its lack of oral activity" (emphasis added). The lack of oral activity of SQ 20,881 is discussed on page 2 of Applicants' specification, and in the references cited therein. It must be emphasized that Applicants' method claims all contain the limitation "orally administering" and Applicants' composition of matter claims are limited by the expression "an oral antihypertensive composition".

The Examiner has taken the position that "Regardless of the mode of administration, the two compounds have been shown to be functionally equivalent with regard to manner and means of activity." Based on the results reported on the second page of Ondetti et al, the compounds of Applicants' formula I are far more active as angiotensin converting enzyme inhibitors than SQ 20,881. The nonapeptide SQ 20,881 is certainly not

"equivalent" to the compounds of Applicants' formula I.

The application as it now stands is believed to be in condition for allowance. Such action is respectfully requested. Should the Examiner have some question about the above response, or should he feel that there are still outstanding issues to resolve, he is respectfully requested to contact the undersigned by phone and arrange for a personal interview.

Respectfully submitted,



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